UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,699	02/03/2006	Gianni Sava	NOTAR-031US	3882

7663 7590 07/14/2008

STETINA BRUNDA GARRED & BRUCKER
75 ENTERPRISE, SUITE 250
ALISO VIEJO, CA 92656

EXAMINER	
WESTERBERG, NISSA M	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
07/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,699	SAVA ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 3 - 5, 26 - 29, 31 - 55* is/are pending in the application.

4a) Of the above claim(s) *37 - 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3 - 5, 26 - 29, 31 - 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/3/06, 5/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I and the required presence of hydroxypropylmethylcellulose (HPMC) in the reply filed on May 22, 2008 is acknowledged. The traversal is on the basis that no lack of unity was found during the international phase of the PCT application and all the groups are unequivocally directed to the same concept.

These arguments are not found to be persuasive. Each case is treated on its own merits and the actions of another office or International Search Authority does not effect the treatment of the case by USPTO. While each group is directed to the same concept (see below for art regarding microcapsules which require chitosan, alginate and HPMC), this concept is known in the art and as the special technical feature must represent a contribution over the prior art, the three groups are therefore not linked by a special technical feature.

The requirement is still deemed proper and is therefore made FINAL.

Comments and Notes

The claims of the elected group are product-by-process claims, in which particular solutions are used to obtain a polysaccharide double-layer microcapsule

having an outer layer of chitosan and an inner layer of alginate with HPMC encapsulating at least one biologically active agent. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) **MPEP 2113**. Therefore, art which discloses microcapsules having an inner alginate/HPMC layer and outer chitosan layer encapsulating at least one biologically active substance, regardless of the process or concentration of the ingredients used in that process, is applied below. While concentrations of ingredients are presented in independent claims 1 and 29, and some steps as to how these solutions are used to prepare the microcapsules are presented in independent claim 29, the claim language is open. Therefore, while the presence of a divalent ion is required, the washing of the microcapsules to remove the divalent ion is not excluded from the claims. In traversing the art rejections presented below, Applicant must provide evidence of an unobvious difference between the claimed product and the prior art product. Please see MPEP 2113 for more information regarding product-by-process claims.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 3, 4, 29, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (J Microencapsulation 2003).

Lee et al. discloses alginate microspheres (microcapsules) which were coated or blended with the polymers HPMC, EUDRAGIT® RS 30D and chitosan (abstract). The encapsulated active ingredient was the calcium channel blocker felodipine (p 181, paragraph 2). Sodium alginate is gelled when contacted with calcium ions in solution (p 179, paragraph 2). Microspheres made from alginate blended with HPMC showed an ideal linear release profile (p 185, paragraph 3) and is a good candidate for controlling drug release (p 185, paragraph 4). Coating of alginate microspheres with chitosan can prevent the swelling and disintegration of alginate microspheres caused by the release of calcium ions (p 189, paragraph 3) and make chitosan coated microspheres suitable for use as a drug delivery vehicle (p 190, paragraph 1). Coating of alginate microspheres with chitosan also provides and smooth and round surface (p 191, paragraph 1 and figure 2(d)).

Lee et al. does not explicitly prepare a microcapsule encapsulating an active ingredient with an inner layer of alginate/HPMC and an outer layer of chitosan.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a microcapsule encapsulating an active ingredient with an inner layer of alginate/HPMC and an outer layer of chitosan as the inner layer, resulting in a microcapsule with an ideal linear release profiled, provided by the composition of the inner layer, with a smooth, round exterior that does not swell and disintegrate upon lose of the calcium, provided the chitosan coating.

6. Claims 1, 3 – 5 , 26, 27, 29 and 31 – 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. as applied to claims 1, 3, 4, 29, 31 and 32 above, and further in view of Illum (US 5,690,954).

Lee et al. discloses microspheres encapsulating a small molecule drug with an inner layer of alginate/HPMC, gelled with calcium, which provides ideal linear release, with an outer chitosan coating that provides a smooth, round microsphere that is not prone to swelling and disintegration upon removal of calcium.

Lee et al. does not disclose other biologically active agents which can be encapsulated by the microsphere.

Illum discloses a microsphere drug delivery system for an active ingredient that also includes a material associated with each particle that increases the bioavailability of the drug (abstract). The enhancing agent or other adjuvants would be expected to provide enhanced bioavailability (col 1, ln 44 – 47). Among the active ingredients that are suitable for inclusion in the delivery system is lysozyme (col 9, ln 35). Lysozyme is identified by Applicant as an immunomodulator (p 6, ln 32 of the instant application). A pharmaceutical adjuvant can be incorporated into or onto a bioadhesive microsphere (col 6, ln 1 – 5).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare an alginate/HPMC/chitosan microsphere as taught by Lee et al. and to use lysozyme as the active ingredient to be delivered by the microspheres,

taught by Illum as an biologically active substance that can be delivered using microspheres.

7. Claims 1, 3 – 5, 27, 29, 31 – 33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. as applied to claims 1, 3, 4, 29, 31 and 32 above, and further in view of Andrianov et al. (US 5,529,777).

Lee et al. discloses microspheres encapsulating a small molecule drug with an inner layer of alginate/HPMC, gelled with calcium, which provides ideal linear release, with an outer chitosan coating that provides a smooth, round microsphere that is not prone to swelling and disintegration upon removal of calcium.

Lee et al. does not disclose the presence of an adjuvant to increase the response of the immune system.

Andrianov et al. discloses the use of microparticles comprised of alginate which can be used to deliver an antigen and therefore are useful as vaccines (abstract). Adjuvants can be added to provoke a strong immune system response when purified antigens are used (col 1, ln 34 – 40) and can be included with the encapsulated antigen (col 13, ln 2 – 4). Polymers, polyelectrolytes and even trace amounts of cholera toxin can function as adjuvants (col 2, ln 65 – col 3, ln 23; col 13, ln 1 – 42).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare an alginate/HPMC/chitosan microsphere, as taught by Lee et al., and to include an antigen and adjuvant as the active ingredients, taught as

suitable active ingredient to be delivered using alginate microspheres, as taught by Andrianov et al., to prepare a composition that can be used as a vaccine.

8. Claims 1, 3 - 5, 26 - 29 and 31 – 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. and Andrianov et al. as applied to claims 1, 3 – 5, 27, 29, 31 – 33 and 35 above, and further in view of Huang et al. (US 2003/0074700).

Lee et al. discloses microspheres encapsulating a small molecule drug with an inner layer of alginate/HPMC, gelled with calcium, which provides ideal linear release, with an outer chitosan coating that provides a smooth, round microsphere that is not prone to swelling and disintegration upon removal of calcium. Andrianov et al. teaches that a purified antigen and adjuvant can be delivered by microsphere and a strong immune response provoked.

Neither Lee et al. nor Andrianov disclose the use of lysozyme as an adjuvant.

Huang et al. discloses that lysozyme has been found to possess a variety of properties, including protection by lysis of microbial cell walls, adjuvant activity of the end products of peptidoglycan lysis and direct immunomodulating effects on leukocytes (paragraph [0268]).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a microsphere are taught by Lee et al. and Andrianov et al. in which an adjuvant and biologically active agent is incorporated in the alginate/HPMC/chitosan microsphere and to use lysozyme as the adjuvant substance,

taught by Huang et al. to be functionally equivalent to the adjuvants described in Andrianov et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW